

SEQUENCE LISTING

<110> Carmeliet, Peter
Moons, Lieve

<120> A NOVEL TARGET TO INHIBIT ANGIOGENESIS

<130> DECLE70.003APC

<150> EP02075544.3

<151> 2002-02-08

<150> EP02077742.1

<151> 2002-07-09

<150> EP03100148.0

<151> 2003-01-24

<160> 2

<170> PatentIn version 3.1

<210> 1

<211> 3794

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (38)..(2635)

<223>

<400> 1

```

ccaagttcta cctcatgttt ggaggatctt gctagct atg gcc ctc gta ctc ggc      55
                                   Met Ala Leu Val Leu Gly
                                   1           5

tcc ctg ttg ctg ctg ggg ctg tgc ggg aac tcc ttt tca gga ggg cag      103
Ser Leu Leu Leu Leu Gly Leu Cys Gly Asn Ser Phe Ser Gly Gly Gln
          10           15           20

cct tca tcc aca gat gct cct aag gct tgg aat tat gaa ttg cct gca      151
Pro Ser Ser Thr Asp Ala Pro Lys Ala Trp Asn Tyr Glu Leu Pro Ala
          25           30           35

aca aat tat gag acc caa gac tcc cat aaa gct gga ccc att ggc att      199
Thr Asn Tyr Glu Thr Gln Asp Ser His Lys Ala Gly Pro Ile Gly Ile
          40           45           50

ctc ttt gaa cta gtg cat atc ttt ctc tat gtg gta cag ccg cgt gat      247
Leu Phe Glu Leu Val His Ile Phe Leu Tyr Val Val Gln Pro Arg Asp
55           60           65           70

ttc cca gaa gat act ttg aga aaa ttc tta cag aag gca tat gaa tcc      295
Phe Pro Glu Asp Thr Leu Arg Lys Phe Leu Gln Lys Ala Tyr Glu Ser
          75           80           85

```

aaa att gat tat gac aag cca gaa act gta atc tta ggt cta aag att Lys Ile Asp Tyr Asp Lys Pro Glu Thr Val Ile Leu Gly Leu Lys Ile 90 95 100	343
gtc tac tat gaa gca ggg att att cta tgc tgt gtc ctg ggg ctg ctg Val Tyr Tyr Glu Ala Gly Ile Ile Leu Cys Cys Val Leu Gly Leu Leu 105 110 115	391
ttt att att ctg atg cct ctg gtg ggg tat ttc ttt tgt atg tgt cgt Phe Ile Ile Leu Met Pro Leu Val Gly Tyr Phe Phe Cys Met Cys Arg 120 125 130	439
tgc tgt aac aaa tgt ggt gga gaa atg cac cag cga cag aag gaa aat Cys Cys Asn Lys Cys Gly Gly Glu Met His Gln Arg Gln Lys Glu Asn 135 140 145 150	487
ggg ccc ttc ctg agg aaa tgc ttt gca atc tcc ctg ttg gtg att tgt Gly Pro Phe Leu Arg Lys Cys Phe Ala Ile Ser Leu Leu Val Ile Cys 155 160 165	535
ata ata ata agc att ggc atc ttc tat ggt ttt gtg gca aat cac cag Ile Ile Ile Ser Ile Gly Ile Phe Tyr Gly Phe Val Ala Asn His Gln 170 175 180	583
gta aga acc cgg atc aaa agg agt cgg aaa ctg gca gat agc aat ttc Val Arg Thr Arg Ile Lys Arg Ser Arg Lys Leu Ala Asp Ser Asn Phe 185 190 195	631
aag gac ttg cga act ctc ttg aat gaa act cca gag caa atc aaa tat Lys Asp Leu Arg Thr Leu Leu Asn Glu Thr Pro Glu Gln Ile Lys Tyr 200 205 210	679
ata ttg gcc cag tac aac act acc aag gac aag gcg ttc aca gat ctg Ile Leu Ala Gln Tyr Asn Thr Thr Lys Asp Lys Ala Phe Thr Asp Leu 215 220 225 230	727
aac agt atc aat tca gtg cta gga ggc gga att ctt gac cga ctg aga Asn Ser Ile Asn Ser Val Leu Gly Gly Gly Ile Leu Asp Arg Leu Arg 235 240 245	775
ccc aac atc atc cct gtt ctt gat gag att aag tcc atg gca aca gcg Pro Asn Ile Ile Pro Val Leu Asp Glu Ile Lys Ser Met Ala Thr Ala 250 255 260	823
atc aag gag acc aaa gag gcg ttg gag aac atg aac agc acc ttg aag Ile Lys Glu Thr Lys Glu Ala Leu Glu Asn Met Asn Ser Thr Leu Lys 265 270 275	871
agc ttg cac caa caa agt aca cag ctt agc agc agt ctg acc agc gtg Ser Leu His Gln Gln Ser Thr Gln Leu Ser Ser Ser Leu Thr Ser Val 280 285 290	919
aaa act agc ctg cgg tca tct ctc aat gac cct ctg tgc ttg gtg cat Lys Thr Ser Leu Arg Ser Ser Leu Asn Asp Pro Leu Cys Leu Val His 295 300 305 310	967

cca tca agt gaa acc tgc aac agc atc aga ttg tct cta agc cag ctg	1015
Pro Ser Ser Glu Thr Cys Asn Ser Ile Arg Leu Ser Leu Ser Gln Leu	
315 320 325	
aat agc aac cct gaa ctg agg cag ctt cca ccc gtg gat gca gaa ctt	1063
Asn Ser Asn Pro Glu Leu Arg Gln Leu Pro Pro Val Asp Ala Glu Leu	
330 335 340	
gac aac gtt aat aac gtt ctt agg aca gat ttg gat ggc ctg gtc caa	1111
Asp Asn Val Asn Asn Val Leu Arg Thr Asp Leu Asp Gly Leu Val Gln	
345 350 355	
cag ggc tat caa tcc ctt aat gat ata cct gac aga gta caa cgc caa	1159
Gln Gly Tyr Gln Ser Leu Asn Asp Ile Pro Asp Arg Val Gln Arg Gln	
360 365 370	
acc acg act gtc gta gca ggt atc aaa agg gtc ttg aat tcc att ggt	1207
Thr Thr Thr Val Val Ala Gly Ile Lys Arg Val Leu Asn Ser Ile Gly	
375 380 385 390	
tca gat atc gac aat gta act cag cgt ctt cct att cag gat ata ctc	1255
Ser Asp Ile Asp Asn Val Thr Gln Arg Leu Pro Ile Gln Asp Ile Leu	
395 400 405	
tca gca ttc tct gtt tat gtt aat aac act gaa agt tac atc cac aga	1303
Ser Ala Phe Ser Val Tyr Val Asn Asn Thr Glu Ser Tyr Ile His Arg	
410 415 420	
aat tta cct aca ttg gaa gag tat gat tca tac tgg tgg ctg ggt ggc	1351
Asn Leu Pro Thr Leu Glu Glu Tyr Asp Ser Tyr Trp Trp Leu Gly Gly	
425 430 435	
ctg gtc atc tgc tct ctg ctg acc ctc atc gtg att ttt tac tac ctg	1399
Leu Val Ile Cys Ser Leu Leu Thr Leu Ile Val Ile Phe Tyr Tyr Leu	
440 445 450	
ggc tta ctg tgt ggc gtg tgc ggc tat gac agg cat gcc acc ccg acc	1447
Gly Leu Leu Cys Gly Val Cys Gly Tyr Asp Arg His Ala Thr Pro Thr	
455 460 465 470	
acc cga ggc tgt gtc tcc aac acc gga ggc gtc ttc ctc atg gtt gga	1495
Thr Arg Gly Cys Val Ser Asn Thr Gly Gly Val Phe Leu Met Val Gly	
475 480 485	
gtt gga tta agt ttc ctc ttt tgc tgg ata ttg atg atc att gtg gtt	1543
Val Gly Leu Ser Phe Leu Phe Cys Trp Ile Leu Met Ile Ile Val Val	
490 495 500	
ctt acc ttt gtc ttt ggt gca aat gtg gaa aaa ctg atc tgt gaa cct	1591
Leu Thr Phe Val Phe Gly Ala Asn Val Glu Lys Leu Ile Cys Glu Pro	
505 510 515	
tac acg agc aag gaa tta ttc cgg gtt ttg gat aca ccc tac tta cta	1639
Tyr Thr Ser Lys Glu Leu Phe Arg Val Leu Asp Thr Pro Tyr Leu Leu	
520 525 530	
aat gaa gac tgg gaa tac tat ctc tct ggg aag cta ttt aat aaa tca	1687

Asn	Glu	Asp	Trp	Glu	Tyr	Tyr	Leu	Ser	Gly	Lys	Leu	Phe	Asn	Lys	Ser		
535					540					545					550		
aaa	atg	aag	ctc	act	ttt	gaa	caa	gtt	tac	agt	gac	tgc	aaa	aaa	aat	1735	
Lys	Met	Lys	Leu	Thr	Phe	Glu	Gln	Val	Tyr	Ser	Asp	Cys	Lys	Lys	Asn		
				555					560					565			
aga	ggc	act	tac	ggc	act	ctt	cac	ctg	cag	aac	agc	ttc	aat	atc	agt	1783	
Arg	Gly	Thr	Tyr	Gly	Thr	Leu	His	Leu	Gln	Asn	Ser	Phe	Asn	Ile	Ser		
			570					575					580				
gaa	cat	ctc	aac	att	aat	gag	cat	act	gga	agc	ata	agc	agt	gaa	ttg	1831	
Glu	His	Leu	Asn	Ile	Asn	Glu	His	Thr	Gly	Ser	Ile	Ser	Ser	Glu	Leu		
		585					590					595					
gaa	agt	ctg	aag	gta	aat	ctt	aat	atc	ttt	ctg	ttg	ggt	gca	gca	gga	1879	
Glu	Ser	Leu	Lys	Val	Asn	Leu	Asn	Ile	Phe	Leu	Leu	Gly	Ala	Ala	Gly		
	600					605					610						
aga	aaa	aac	ctt	cag	gat	ttt	gct	gct	tgt	gga	ata	gac	aga	atg	aat	1927	
Arg	Lys	Asn	Leu	Gln	Asp	Phe	Ala	Ala	Cys	Gly	Ile	Asp	Arg	Met	Asn		
	615				620					625					630		
tat	gac	agc	tac	ttg	gct	cag	act	ggc	aaa	tcc	ccc	gca	gga	gtg	aat	1975	
Tyr	Asp	Ser	Tyr	Leu	Ala	Gln	Thr	Gly	Lys	Ser	Pro	Ala	Gly	Val	Asn		
				635					640					645			
ctt	tta	tca	ttt	gca	tat	gat	cta	gaa	gca	aaa	gca	aac	agt	ttg	ccc	2023	
Leu	Leu	Ser	Phe	Ala	Tyr	Asp	Leu	Glu	Ala	Lys	Ala	Asn	Ser	Leu	Pro		
			650					655					660				
cca	gga	aat	ttg	agg	aac	tcc	ctg	aaa	aga	gat	gca	caa	act	att	aaa	2071	
Pro	Gly	Asn	Leu	Arg	Asn	Ser	Leu	Lys	Arg	Asp	Ala	Gln	Thr	Ile	Lys		
		665					670					675					
aca	att	cac	cag	caa	cga	gtc	ctt	cct	ata	gaa	caa	tca	ctg	agc	act	2119	
Thr	Ile	His	Gln	Gln	Arg	Val	Leu	Pro	Ile	Glu	Gln	Ser	Leu	Ser	Thr		
	680					685					690						
cta	tac	caa	agc	gtc	aag	ata	ctt	caa	cgc	aca	ggg	aat	gga	ttg	ttg	2167	
Leu	Tyr	Gln	Ser	Val	Lys	Ile	Leu	Gln	Arg	Thr	Gly	Asn	Gly	Leu	Leu		
	695				700				705					710			
gag	aga	gta	act	agg	att	cta	gct	tct	ctg	gat	ttt	gct	cag	aac	ttc	2215	
Glu	Arg	Val	Thr	Arg	Ile	Leu	Ala	Ser	Leu	Asp	Phe	Ala	Gln	Asn	Phe		
				715					720					725			
atc	aca	aac	aat	act	tcc	tct	gtt	att	att	gag	gaa	act	aag	aag	tat	2263	
Ile	Thr	Asn	Asn	Thr	Ser	Ser	Val	Ile	Ile	Glu	Glu	Thr	Lys	Lys	Tyr		
			730					735					740				
ggg	aga	aca	ata	ata	gga	tat	ttt	gaa	cat	tat	ctg	cag	tgg	atc	gag	2311	
Gly	Arg	Thr	Ile	Ile	Gly	Tyr	Phe	Glu	His	Tyr	Leu	Gln	Trp	Ile	Glu		
		745					750					755					
ttc	tct	atc	agt	gag	aaa	gtg	gca	tcg	tgc	aaa	cct	gtg	gcc	acc	gct	2359	
Phe	Ser	Ile	Ser	Glu	Lys	Val	Ala	Ser	Cys	Lys	Pro	Val	Ala	Thr	Ala		

760	765	770	
cta gat act gct gtt gat gtc ttt ctg tgt agc tac att atc gac ccc			2407
Leu Asp Thr Ala Val Asp Val Phe Leu Cys Ser Tyr Ile Ile Asp Pro			
775	780	785	790
ttg aat ttg ttt tgg ttt ggc ata gga aaa gct act gta ttt tta ctt			2455
Leu Asn Leu Phe Trp Phe Gly Ile Gly Lys Ala Thr Val Phe Leu Leu			
	795	800	805
ccg gct cta att ttt gcg gta aaa ctg gct aag tac tat cgt cga atg			2503
Pro Ala Leu Ile Phe Ala Val Lys Leu Ala Lys Tyr Tyr Arg Arg Met			
	810	815	820
gat tcg gag gac gtg tac gat gat gtt gaa act ata ccc atg aaa aat			2551
Asp Ser Glu Asp Val Tyr Asp Asp Val Glu Thr Ile Pro Met Lys Asn			
	825	830	835
atg gaa aat ggt aat aat ggt tat cat aaa gat cat gta tat ggt att			2599
Met Glu Asn Gly Asn Asn Gly Tyr His Lys Asp His Val Tyr Gly Ile			
	840	845	850
cac aat cct gtt atg aca agc cca tca caa cat tga tagctgatgt			2645
His Asn Pro Val Met Thr Ser Pro Ser Gln His			
855	860	865	
tgaaactgct tgagcatcag gataactcaaa gtggaaagga tcacagattt ttggtagttt			2705
ctgggtctac aaggactttc caaatccagg agcaacgcca gtggcaacgt agtgactcag			2765
gcgggcacca aggcaacggc accattggtc tctgggtagt gctttaagaa tgaacacaat			2825
cacgttatag tccatgggtcc atcactattc aaggatgact ccctcccttc ctgtctattt			2885
ttgttttttta cttttttaca ctgagtttct atttagacac tacaacatat ggggtgtttg			2945
ttcccattgg atgcatttct atcaaaactc tatcaaagt gatggctaga ttctaacata			3005
ttgccatgtg tggagtgtgc tgaacacaca ccagtttaca ggaaagatgc attttgtgta			3065
cagtaaacgg tgtatatacc ttttgttacc acagagtttt ttaaacaat gagtattata			3125
ggactttctt ctaaagagc taaataagtc accattgact tcttggtgct gttgaaaata			3185
atccattttc actaaaagtg tgtgaaacct acagcatatt cttcacgcag agattttcat			3245
ctattatact ttatcaaaga ttggccatgt tccacttgga aatggcatgc aaaagccatc			3305
atagagaaac ctgcgtaact ccatctgaca aattcaaaag agagagagag atcttgagag			3365
agaaatgctg ttcgttcaaa agtggagtgt ttttaacaga tgccaattac ggtgtacagt			3425
ttaacagagt tttctgttgc attaggataa acattaattg gagtgcagct aacatgagta			3485
tcatacagact agtatcaagt gttctaaaat gaaatatgag aagatcctgt cacaattctt			3545
agatctggtg tccagcatgg atgaaacct tgagtttggt ccctaaattt gcatgaaagc			3605

acaaggtaaa tattcatttg cttcaggagt ttcattgttg atctgtcatt atcaaaagtg 3665
atcagcaatg aagaactggg cggacaaaat ttaacgttga tgtaatggaa ttccagatgt 3725
aggcattccc cccaggtctt ttcattgtga gattgcagtt ctgattcatt tgaataaaaa 3785
ggaacttgg 3794

<210> 2
<211> 865
<212> PRT
<213> Homo sapiens

<400> 2

Met Ala Leu Val Leu Gly Ser Leu Leu Leu Leu Gly Leu Cys Gly Asn
1 5 10 15

Ser Phe Ser Gly Gly Gln Pro Ser Ser Thr Asp Ala Pro Lys Ala Trp
20 25 30

Asn Tyr Glu Leu Pro Ala Thr Asn Tyr Glu Thr Gln Asp Ser His Lys
35 40 45

Ala Gly Pro Ile Gly Ile Leu Phe Glu Leu Val His Ile Phe Leu Tyr
50 55 60

Val Val Gln Pro Arg Asp Phe Pro Glu Asp Thr Leu Arg Lys Phe Leu
65 70 75 80

Gln Lys Ala Tyr Glu Ser Lys Ile Asp Tyr Asp Lys Pro Glu Thr Val
85 90 95

Ile Leu Gly Leu Lys Ile Val Tyr Tyr Glu Ala Gly Ile Ile Leu Cys
100 105 110

Cys Val Leu Gly Leu Leu Phe Ile Ile Leu Met Pro Leu Val Gly Tyr
115 120 125

Phe Phe Cys Met Cys Arg Cys Cys Asn Lys Cys Gly Gly Glu Met His
130 135 140

Gln Arg Gln Lys Glu Asn Gly Pro Phe Leu Arg Lys Cys Phe Ala Ile
145 150 155 160

Ser Leu Leu Val Ile Cys Ile Ile Ile Ser Ile Gly Ile Phe Tyr Gly
165 170 175

Phe Val Ala Asn His Gln Val Arg Thr Arg Ile Lys Arg Ser Arg Lys
180 185 190

Leu Ala Asp Ser Asn Phe Lys Asp Leu Arg Thr Leu Leu Asn Glu Thr
195 200 205

Pro Glu Gln Ile Lys Tyr Ile Leu Ala Gln Tyr Asn Thr Thr Lys Asp
210 215 220

Lys Ala Phe Thr Asp Leu Asn Ser Ile Asn Ser Val Leu Gly Gly Gly
225 230 235 240

Ile Leu Asp Arg Leu Arg Pro Asn Ile Ile Pro Val Leu Asp Glu Ile
245 250 255

Lys Ser Met Ala Thr Ala Ile Lys Glu Thr Lys Glu Ala Leu Glu Asn
260 265 270

Met Asn Ser Thr Leu Lys Ser Leu His Gln Gln Ser Thr Gln Leu Ser
275 280 285

Ser Ser Leu Thr Ser Val Lys Thr Ser Leu Arg Ser Ser Leu Asn Asp
290 295 300

Pro Leu Cys Leu Val His Pro Ser Ser Glu Thr Cys Asn Ser Ile Arg
305 310 315 320

Leu Ser Leu Ser Gln Leu Asn Ser Asn Pro Glu Leu Arg Gln Leu Pro
325 330 335

Pro Val Asp Ala Glu Leu Asp Asn Val Asn Asn Val Leu Arg Thr Asp
340 345 350

Leu Asp Gly Leu Val Gln Gln Gly Tyr Gln Ser Leu Asn Asp Ile Pro
355 360 365

Asp Arg Val Gln Arg Gln Thr Thr Thr Val Val Ala Gly Ile Lys Arg
370 375 380

Val Leu Asn Ser Ile Gly Ser Asp Ile Asp Asn Val Thr Gln Arg Leu

385		390		395		400									
Pro	Ile	Gln	Asp	Ile	Leu	Ser	Ala	Phe	Ser	Val	Tyr	Val	Asn	Asn	Thr
			405						410					415	
Glu	Ser	Tyr	Ile	His	Arg	Asn	Leu	Pro	Thr	Leu	Glu	Glu	Tyr	Asp	Ser
			420					425					430		
Tyr	Trp	Trp	Leu	Gly	Gly	Leu	Val	Ile	Cys	Ser	Leu	Leu	Thr	Leu	Ile
		435					440					445			
Val	Ile	Phe	Tyr	Tyr	Leu	Gly	Leu	Leu	Cys	Gly	Val	Cys	Gly	Tyr	Asp
	450					455					460				
Arg	His	Ala	Thr	Pro	Thr	Thr	Arg	Gly	Cys	Val	Ser	Asn	Thr	Gly	Gly
465					470					475					480
Val	Phe	Leu	Met	Val	Gly	Val	Gly	Leu	Ser	Phe	Leu	Phe	Cys	Trp	Ile
			485						490					495	
Leu	Met	Ile	Ile	Val	Val	Leu	Thr	Phe	Val	Phe	Gly	Ala	Asn	Val	Glu
			500					505					510		
Lys	Leu	Ile	Cys	Glu	Pro	Tyr	Thr	Ser	Lys	Glu	Leu	Phe	Arg	Val	Leu
		515					520					525			
Asp	Thr	Pro	Tyr	Leu	Leu	Asn	Glu	Asp	Trp	Glu	Tyr	Tyr	Leu	Ser	Gly
	530					535					540				
Lys	Leu	Phe	Asn	Lys	Ser	Lys	Met	Lys	Leu	Thr	Phe	Glu	Gln	Val	Tyr
545				550					555						560
Ser	Asp	Cys	Lys	Lys	Asn	Arg	Gly	Thr	Tyr	Gly	Thr	Leu	His	Leu	Gln
			565						570					575	
Asn	Ser	Phe	Asn	Ile	Ser	Glu	His	Leu	Asn	Ile	Asn	Glu	His	Thr	Gly
			580					585					590		
Ser	Ile	Ser	Ser	Glu	Leu	Glu	Ser	Leu	Lys	Val	Asn	Leu	Asn	Ile	Phe
		595					600					605			
Leu	Leu	Gly	Ala	Ala	Gly	Arg	Lys	Asn	Leu	Gln	Asp	Phe	Ala	Ala	Cys
	610					615					620				

Gly Ile Asp Arg Met Asn Tyr Asp Ser Tyr Leu Ala Gln Thr Gly Lys
 625 630 635 640

Ser Pro Ala Gly Val Asn Leu Leu Ser Phe Ala Tyr Asp Leu Glu Ala
 645 650 655

Lys Ala Asn Ser Leu Pro Pro Gly Asn Leu Arg Asn Ser Leu Lys Arg
 660 665 670

Asp Ala Gln Thr Ile Lys Thr Ile His Gln Gln Arg Val Leu Pro Ile
 675 680 685

Glu Gln Ser Leu Ser Thr Leu Tyr Gln Ser Val Lys Ile Leu Gln Arg
 690 695 700

Thr Gly Asn Gly Leu Leu Glu Arg Val Thr Arg Ile Leu Ala Ser Leu
 705 710 715 720

Asp Phe Ala Gln Asn Phe Ile Thr Asn Asn Thr Ser Ser Val Ile Ile
 725 730 735

Glu Glu Thr Lys Lys Tyr Gly Arg Thr Ile Ile Gly Tyr Phe Glu His
 740 745 750

Tyr Leu Gln Trp Ile Glu Phe Ser Ile Ser Glu Lys Val Ala Ser Cys
 755 760 765

Lys Pro Val Ala Thr Ala Leu Asp Thr Ala Val Asp Val Phe Leu Cys
 770 775 780

Ser Tyr Ile Ile Asp Pro Leu Asn Leu Phe Trp Phe Gly Ile Gly Lys
 785 790 795 800

Ala Thr Val Phe Leu Leu Pro Ala Leu Ile Phe Ala Val Lys Leu Ala
 805 810 815

Lys Tyr Tyr Arg Arg Met Asp Ser Glu Asp Val Tyr Asp Asp Val Glu
 820 825 830

Thr Ile Pro Met Lys Asn Met Glu Asn Gly Asn Asn Gly Tyr His Lys
 835 840 845

Asp His Val Tyr Gly Ile His Asn Pro Val Met Thr Ser Pro Ser Gln
850 855 860

His
865